REMARKS

Claims 14-25 are pending in the present application.

The rejection of Claim 19 under 35 U.S.C. §112, first paragraph (enablement), is obviated in part and traversed in part.

The Examiner has rejected Claim 19 as lacking sufficient enablement for four apparent reasons: (1) the scope of the HLA molecule and the peptide bound thereto, (2) an alleged insufficiency in the disclosure of the "effective amount" of activated CTL, (3) an alleged omission of evidence that *in vitro* activated CTL elicits an *in vivo* prophylactic or therapeutic effect, and (4) an alleged omission of a disclosed method to allow expansion of a specific tumor specific CTL clone without losing its specificity (see paragraph bridging pages 4 and 5 of the Office Action mailed January 15, 2004). Applicants disagree with these assertions and address each point below.

In regard to point (1) above, the Examiner contends that "the specification as filed fails to disclose all gastric cancer specific peptides that bind to all types of HLA molecule to induce a CTL response against the target gastric cancer cells in-vitro or in-vivo." Surely the Examiner recognizes that no precedent exists either in the common law, the rules, the code, or the MPEP that Applicant must disclose *all* variants/species of a genus. Nonetheless, Applicants make no statement regarding the propriety of this basis for rejection and in no way acquiesce to the same. However, for the sake of expedient prosecution, Applicants have amended Claim 19 to define the HLA molecule as HLA-A31. In addition, Claim 19 has been amended to define the peptide bound to HLA-A31 as being:

(a) A peptide which is a fragment of a gastric cancer antigen protein present in a human gastric cancer cell wherein said peptide comprises SEQ. ID. NO. 1 and consists of 10-12 amino acid residues, or

(b) A peptide which is a fragment of a gastric cancer antigen protein present in a human gastric cancer cell wherein said peptide comprises SEQ. ID. NO. 2 and consists of 9-12 amino acid residues.

Therefore, in view of the foregoing, Applicants submit that point (1) is no longer applicable.

In regard to (2), the U.S. Courts have routinely held the phrase "an effective amount" to be definite when the amount is not critical and those skilled in the art would be able to determine from the written disclosure, including the examples, what an effective amount is (MPEP §2173.05(b)). In the present application, the term "an effective amount" refers to an amount effective for the prevention or treatment of gastric cancer. Accordingly, Applicants submit that it is well within the purview of the skilled artisan to determine what an effective amount is for the claimed use when determined in light of the guidance provided by the specification and the level of ordinary skill in the art.

Turning to point (3), Applicants disagree with the assertion that the skilled artisan would have no guidance that *in vitro* activated CTL elicits an *in vivo* prophylactic or therapeutic effect. MPEP § 2164.01 states:

> The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.

Applicants note that the specification clearly discloses administering *in vitro* activated CTL to a patient in need thereof appears on page 17, lines 23 to page 18, line 3. Moreover, at this point, the specification sets forth: "the treatment through such a cell transfer has been

already practiced as a cancer therapy, and it is well known to those skilled in the art." Accordingly, to evidence that the skilled artisan may practice the claimed invention from the disclosures in the present specification coupled with information known in the art without undue experimentation, Applicants **submit herewith** the following three references:

1) Rosenberg, et al., New Eng. J. Med., 319(25), 1676-1680 (1988);

2) Toh, et al., Clin. Cancer Res., 6, 4663-4673 (2000); and

3) Dudley, et al., Science, 298, 850-854 (2002).

These references evince the effectiveness of cancer immunotherapy using tumor antigens. As set forth in these references, there are many examples of immunotherapy using tumor antigens and, therefore, the skilled artisan would readily appreciate selection of effective antigens as presently claimed. To ensure clarity of the claimed invention, Claim 19 has been amended based on the specification at page 17, lines 23 to page 18, line 3 to specify the *in vitro* activation of CTL by adding the activating peptide to lymphocytes of the patient in need of prevention and/or treatment of gastric cancer. Subsequently the activated CTL is returned to the *same* patient to effectuate cancer prophylaxis or cancer therapy.

Moreover, Applicants direct the Examiner's attention to Nabeta, et al., Jpn. J. Cancer Res., 91, 616-621 (2000), in which the present inventors have demonstrated that immunotherapy has a significant rate of recovery compared to mortality. Therefore, immunotherapy does possess efficacious advantages.

Finally, in regard to point (4), Applicants submit that the presence or absence of methods to allow expansion of a specific tumor specific CTL clone without losing its specificity is irrelevant in the analysis of whether Claim 19 is enabled by the disclosure of the present specification. Specifically, Applicants note that the claimed invention pertains to a method of preventing or treating gastric cancer by administering an effective amount of activated CTL, the method by which the tumor-specific CTL clone is obtained is not limiting.

Moreover, Applicants note that page 10, line 16 to page 11, line 2 refer the artisan to several references that disclose methods for tumor-specific CTL cell strain expansion. For the Examiner's convenience, the following cited references are **enclosed herewith**:

1) Wada, et al., J. Immunol. Meth., 154, 235-243 (1992);

2) Wada, et al., Jpn. J. Cancer Res., 84, 906-913 (1993); and

3) Yasashima, et al., Cancer, 75, 1484-1489 (1995).

Based on the foregoing, Applicants submit that the present claims are fully enabled by the specification and the common knowledge available in the art and as such withdrawal of this ground of rejection is requested.

Applicants wish to thank Examiner Kaushal for the kind suggestion to obtain the benefit of an earlier filing date under 35 U.S.C. §120. Consistent with this indication, the specification has been amended to include the requisite priority statement. Applicants request that the Office acknowledge the benefit of priority under 35 U.S.C. §120 in the next action.

Applicants submit that the present application is now in condition for allowance.

Early notification of such action is earnestly solicited.

Respectfully submitted,

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